Blood Cell Profiles of Malaria Patients Attending Gaya General Hospital, Kano State, Northern Nigeria

ABSTRACT

***Background**: In the rural community of Kano State, Nigeria, information on haematological changes in human malaria was scanty in spite of their role in the pathophysiology of malaria. This cross-sectional study was undertaken to determine blood cell profiles of suspected malarial patients attending a rural hospital in malaria-endemic region.*

***Methods**: Blood samples (3ml each) were collected in EDTA-containers from 150 randomly selected outpatients attending Gaya General Hospital, screened for malaria using RDT kit based on Histidine-rich protein 2 (PfHRP-2), and blood cell profiles determined using automated Sysmex haematologic analyser. Data on medical history related to the study objectives (taking antimalarial regimen and/or haematinic, and direct involvement in blood transfusion, etc.) were obtained through interview and questionnaire administration.*

***Findings**: Malaria prevalence of 67.33%, which was highest in 11-20years (80.95%) and lowest (55.00%) in 1-10years age-groups, and higher in females (68.25%) than in males (66.67%) was recorded without significant difference ($P>0.05$). For blood parameters, malaria positive patients have a significantly lower mean PCV of 32.2% as compared to 38.18% obtained for malaria negative patients ($P<0.05$). The mean Hb was 10.76±2.27g/dL and 12.65±2.38g/dL ($P<0.05$), while WBC revealed 6.91×10^9/L and 6.56×10^9/L in malaria positive and negative patients, respectively. Platelet counts recorded 179.24×10^9/L and 230.47×10^9/L ($P<0.05$).*

***Interpretation**: Low PCV and Hb in malaria positive cases are indicative of mild anaemia due to malaria-related haemolysis, without prejudice to the observed low counts in WBC and Platelets due to Plasmodium infection in humans, a situation likely to be found in such malaria-endemic settings.*

***Keywords**: Malaria prevalence, Blood parameters, Anaemia, Rural community*

INTRODUCTION

Human malaria is a mosquito-borne infectious disease caused by parasitic protozoans belonging to the genus *Plasmodium*.[1] Malaria causes symptoms that typically include fever, fatigue, vomiting, and headaches. In severe cases it can cause yellow skin, seizures, coma, or death.[2] The disease is most commonly transmitted by an infected female *Anopheles* mosquito. The mosquito bite introduces the parasites from the mosquito's saliva into a person's blood.[1] Four primary species of malaria parasites infect humans: *Plasmodium falciparum, P. ovale, P. malariae* and *P. vivax*. In addition, studies in Southeast Asia have shown that *P. knowlesi*, a malaria parasite that typically infects monkeys as the natural reservoir, can also infect humans, and in some cases, result in fatal disease.[3] Malaria due to *P. vivax, P. ovale* and *P. malariae* is less severe than that experienced by *P. falciparum* infections and collectively, these three species account for slightly less than 10% of the worldwide malaria cases.[4] The most virulent of the human malaria parasites is therefore *Plasmodium falciparum* which is responsible for the bulk of the malaria-related morbidity and mortality. *P. falciparum* accounts for 91% of malaria cases worldwide of which the majority (with about 86%) occurs in the African region.[4] Consistent with the high rate of morbidity within Africa, 90% of the *P. falciparum* attributable-malaria deaths also occur in the African region, primarily sub-Saharan Africa.[4] Malaria is currently endemic in the tropical zones

with extensions into the sub-tropical regions of Asia, Africa, South and Central America. Nigeria suffers the world's greatest malaria burden, with approximately 51 million cases and 207,000 deaths reported annually (approximately 30% of the total malaria burden in Africa), while 97% of the total population (approximately 173 million) is at risk of infection.[5] Haematological changes are some of the most common complications in malaria as the changes involve the major cell lines such as red blood cells, leucocytes, and thrombocytes.[6] Haematological abnormalities are considered a hallmark of malaria and many of these haematological values may lead to increased clinical suspicion for malaria, thus initiating a prompt institution of specific therapy even in the absence of a positive smear report for malaria. Prediction of the haematological changes enables the clinician to establish an effective and early therapeutic intervention in order to prevent the occurrence of major complications. These parameters are measurable indices of blood that serve as a marker for disease diagnosis.[7] In the rural area of Kano State, where the study was undertaken information on haematological changes occurring in malaria patients is scanty in spite of their roles in the pathophysiology of malaria, hence the need to determine the profile of blood cells in malaria patients attending Gaya General Hospital, Kano State, north-western Nigeria, with a view to evaluating the extent of haematological changes associated with malaria in the study area.

MATERIALS AND METHODS

Study Area

The study was carried out at Gaya General Hospital in Gaya Local Government Area of Kano State, Nigeria, which is located between latitude 11.87°N and longitude 9.01°E. It is surrounded by three local government areas, namely; Ajingi to the north, Albasu to the south and Wudil to the west. It has an area of 613 km² and a population of 201,016 at the 2006 population census.[8]

Study Population

The study population comprised 150 patients, out of which 87 were males and 63 were females and of various age categories that had been attending outpatient department of Gaya General Hospital and were prescribed blood malaria test by the medical practitioners upon presentation with high fever and other symptoms suspected of having malaria. The patients came from within and the neighbourhood of the local government area, and mainly from poor family with simple trading and peasant farming as the major occupation of subsistence.

Ethical Clearance

Ethical clearance and approval were obtained from the management of Gaya General Hospital following submission of letter of introduction from the Department of Biology, Kano University of Science and Technology, Wudil. Furthermore, informed consent was obtained directly from adult patients and parents or guardians for non-adults. The participants were assured of confidentiality of the information given which would be used strictly for the purpose of the study.

Inclusion and Exclusion Criteria

All patients who were clinically suspected of having malaria and were prescribed blood malaria confirmatory test during the period of the research and agreed to participate and gave informed consent were included in the study. Patients who did not present with symptoms of malaria and those that presented with malaria symptoms but were taking haematinics, antimalarial drugs or had involved in blood transfusion in recent time (previous 10-14 days) were excluded from the

study. Female patients who were pregnant within the period of the study were also excluded from the study.

Questionnaire Administration

A structured questionnaire was designed for the purpose of the research and administered to the participating individuals of different age groups and both sexes, who had agreed voluntarily to participate in the study. The questionnaire contained the necessary information relevant to the study objectives which included history of blood transfusion, taking of blood tonics and antimalarial treatment. Information contained in the questionnaire was translated into local dialect to poster understanding and facilitate appropriate response. Where necessary an oral interview was employed to supplement the administration of the questionnaire.

Collection of Blood Samples

The subjects enrolled for the study were 150 who were randomly selected and of various age and sex categories. Using 5ml disposable syringe, 2-3ml blood sample was collected from each consented individual suspected of having malaria, put into a well labelled ethylene diamine tetra-acetic acid (EDTA) bottle, and sent to the laboratory for malaria parasite confirmatory test and blood cell profiling. Using the procedure by Cheesbrough[9] the venepuncture site was disinfected with 70% ethanol to cleanse the area of about 50mm in diameter, prior to blood collection. A tourniquet was used to tie the arm of the individual so as to locate the suitable vein in the arm. The collected blood samples were then stored until use.

Determination of Malaria Parasites

Rapid Diagnostic Test (RDT) kit was used to test for the presence of *Plasmodium* antigen (P*f*HRP-2) in the blood samples. A drop of blood sample was dropped into a square hole and buffer added into a round hole on the kit. Appearance of double lines (control and test lines) indicated the presence of *Plasmodium* antigen; a positive result, while appearance of a single line (control line) only indicated the absence of *Plasmodium* antigen; a negative result.

Determination of Haematological Parameters

Packed Cell Volume (PCV): Capillary tubes were used to take the blood samples. Three-quarter of the capillary tube was filled with blood and then sealed from the side of collection. The samples were then centrifuged at 2000rpm in a haematocrit machine for 5 minutes to separate the blood plasma and the blood cells. Haematocrit reader was used to read the percentage of the red blood cells. Other blood parameters such as white blood cell count (WBC), platelets count and haemoglobin concentrations were determined using an automated haematologic analyser (Sysmex KX-21N).

Data Analysis

The data collected were analysed using simple frequencies, means and percentages. Moreover, comparative analysis of the parameters was carried out using chi-square test at 5% level of significance. All data analyses were run by Microsoft Excel, 2007.

RESULTS

Prevalence of Malaria in the Study Population

The result in Table 1 shows the prevalence of malaria in relation to age groups of patients attending Gaya General Hospital. The result shows that the age group 11-20years had the highest prevalence of 80.95% while the age group 1-10years had the least malaria prevalence of 55.00%; the overall prevalence of malaria being 67.33%. The result in Table 2 shows sex-related malaria prevalence, with females having a slightly higher prevalence of 68.25% than males with 66.67%. Both age- and sex-related prevalence were not statistically significant at $P<0.05$.

Effect of Malaria on Haematological Parameters

The result for the mean PCV value for malaria-positive individuals was 33.67% and 30.37% for males and females respectively. However, for malaria-negative individuals, males and female had slightly higher PCV values of 39.72% and 35.95% respectively (Table 3). Table 4 shows the effect of malaria on packed cell volume. The prevalence of anaemia and normal PCV in malaria-infected patients is 81(84.38%) and 20(37.04%) respectively. The result reveals a statistically significant difference at 5% level of significance ($P<0.05$). The mean Hb concentration for malaria-positive individuals also varied with sex, with males having 11.26g/dL and females 10.1g/dL. Nonetheless, the Hb concentration for malaria-negative individuals followed a similar pattern with males recording 13.23g/dL and females 11.81g/dL. The result in Table 5 shows the effects of malaria on haemoglobin concentration. There was a significant difference in the haemoglobin concentration between malaria positive and negative cases at $P<0.05$. The prevalence of anaemia in malaria positive patients is 77(81.08%) and normal haemoglobin has prevalence rate of 24 (43.64%). The slight decrease in the mean PCV and Hb in malaria-positive individuals indicated the development of mild anaemia. Moreover, the mean WBC Counts for malaria-positive individuals were 6.87×10^9/L and 6.97×10^9/L for males and females respectively; females having slightly higher value. On the other hand, the mean WBC Counts for malaria-negative individuals were 6.76×10^9/L and 6.26×10^9/L for male and female respectively, showing a slight increase in the study subjects. However, both malaria-positive and malaria-negative individuals have white blood cells counts within normal range. The result in Table 6 shows the effect of malaria on white blood cells. The prevalence of low WBC was 33 (71.74%), normal WBC 54 (61.36%) and High WBC was 14 (87.5%), although, with no statistical significance ($P>0.05$). The mean Platelet Counts for malaria-positive individuals were 190.98×10^9/L and 163.4×10^9/L for males and females respectively. However, the Platelet Counts recorded for malaria-negative individuals were 228.66×10^9/L and 233.1×10^9/L for males and females respectively. There was a marked reduction in Platelet Counts in malaria-positive females compared to the males. The Platelet counts in the study subjects reveal a normal platelets count in 22 (38.6%), thrombocytopenia 75 (85.23%) and thrombocytosis 4 (80%), with statistical significance at $P<0.05$, indicating the effect of malaria on blood platelets count (Table 7).

Table 1: **Prevalence of malaria in relation to age groups**

Age Group(years)	No. Examined	No. Infected	% Prevalence
1-10	20	11	55.00
11-20	21	17	80.95
21-30	30	18	60.00
31-40	34	25	73.53
41-50	17	13	76.47
51-60	16	10	62.50
≥61	12	7	58.33
Total	150	101	67.33

$\chi^2= 54.59$, df= 1, $P= 0.06$

Table 2: **Prevalence of malaria in relation to sex**

Sex	No. Examined	No. Infected	% Prevalence

Male	87	58	66.67
Female	63	43	68.25
Total	150	101	67.33

χ^2= 0.042, df= 1, *P*= 0.08

Table 3: **Mean values of haematological parameters in malaria and non-malaria cases**

	Malaria Positive		**Malaria Negative**	
Parameters*	**Male**	**Female**	**Male**	**Female**
PCV (%)	33.67±6.77	30.37 ±6.54	39.72 ±7.24	35.95 ±6.36
Hb (g/dL)	11.26 ±2.26	10.1 ±2.14	13.23 ±2.39	11.81 ±2.14
WBC ($\times10^9$/L)	6.87 ±4.02	6.97 ±4.7	6.76 ±3.68	6.26 ±2.29
Platelets ($\times10^9$/L)	190.98 ±129.1	163.4 ±99.38	228.66 ±102.5	233.1 ±76.7

***Normal ranges**: PCV: 37-47% (Female), 42-50% (Male); Hb: 12.0-16.0g/dL (Female), 14.0-18.0 g/dL (Male); WBC: 4.0-11.0$\times10^9$/L; Platelets: 200-350$\times10^9$/L
Source: ABIM[10]; Waugh and Grant[11]

Table 4: **Effect of malaria on packed cell volume (PCV)**

PCV	**No. Examined**	**No. Infected**	**% Prevalence**
Mild Anaemia	96	81	84.38
Normal PCV	54	20	37.04
Total	150	101	67.33

χ^2= 35.21, df= 1, *P*= 0.00

Table 5: **Effect of malaria on haemoglobin concentration**

Hb Concentration	**No. Examined**	**No. Infected**	**% Prevalence**
Mild Anaemia	95	77	81.08
Normal Hb Conc.	55	24	43.64
Total	150	101	67.33

χ^2= 22.17, df= 1, *P*= 0.00

Table 6: **Effect of malaria on white blood cells (WBCs)**.

WBC Count	**No. Examined**	**No. Infected**	**% Prevalence**
Low WBC	46	33	71.74
Normal Count	88	54	61.36
High WBC	16	14	87.50
Total	150	101	67.33

χ^2= 4.79, df= 2, *P*= 0.09

Table 7: **Effect of malaria on blood platelets**

Platelet Count	**No. Examined**	**No. Infected**	**% Prevalence**

Thrombocytopenia	88	75	85.23
Normal Count	57	22	38.6
Thrombocytosis	5	4	80.0
Total	150	101	67.33

χ^2= 34.58, df= 2, *P*= 0.00

DISCUSSION

Malaria is one of the most widespread infectious diseases among humans and a common parasitic disease of tropical and subtropical regions of the world. WHO estimated 198 million cases and about 6 million deaths due to malaria in 2013.[1] Hay *et al*.[12] had earlier reported that about 90% of all malaria deaths in the world occur in Africa south of the Sahara. This is due to the fact that the majority of infections in the regions are caused by *Plasmodium falciparum*, the most virulent of the five human malaria parasites and to the presence in the region of the most effective malaria vector, *Anopheles gambiae* complex, which is the most widespread and most difficult to control.[13] The recorded overall malaria prevalence in the study population of 67.33% was high. The presence of competent mosquito vectors in the study area, coupled with inadequate preventive measures from repeated mosquito bites, development of unacceptable levels of resistance to antimalarials in spite of treatment and insecticidal resistance in malaria vector, probably account for this high prevalence in the study population, an observation which is in conformity with the report of WHO[13] that malaria parasites are developing unacceptable levels of resistance to one drug after another and many insecticides are no longer useful against mosquitoes transmitting the disease. Consistent with the present findings, previous studies from Kano State showed high malaria prevalence of 62.5% in patients attending two hospitals in Kano metropolis and 51.7% in pregnant women attending antenatal clinic a specialist hospital were malaria-positive.[5] Moreover, Dawaki *et al*.[5] reported high malaria prevalence among children in Kebbi (64.0%), Awka (59.6%), and Abuja (58.0%). The findings in this study further indicated lack of influence of age of the subjects on the prevalence of malaria. It may therefore be adduced that it is the degree and efficiency of preventive strategies available at community level as well as the subject susceptibility and amount of exposure to infectious mosquito bite, along with other prevailing risk factors for malaria transmission that determine malaria prevalence in the study population. This observation corroborated the findings of WHO[13] who reported that most adults living in malaria endemic areas have partial immunity and are at risk of chronic or repeated infections, and according to Madaki and Zoakah[14] approximately 50% of Nigerian population experience at least one episode of malaria annually. Similarly, the findings of the study showed no gender difference in malaria prevalence, suggesting an equal predisposition of male and female individuals to mosquito bite and, possibly, equal susceptibility to *Plasmodium* infection. However, in another research reported by Dawaki *et al*.[5] a prevalence rate of 60.6% for falciparum malaria was recorded which differed significantly by age-group (P<00.1), but not by gender. Changes in blood cells profile in malaria infections are well recognized, but specific changes may vary with level of malaria, background hemoglobinopathy, nutritional status, demographic factors and malaria immunity.[15] Haematological changes are some of the most common complications in malaria as the changes involve the major cell lines such as red blood cells, white blood cells, and platelets.[6] Hematological abnormalities are considered a hallmark of malaria and statistical analyses have shown that many of these hematological values may lead to an increased clinical suspicion for malaria, thus initiating a prompt institution of specific therapy even in the absence of a positive blood smear report for malaria. Prediction of the hematological

changes enables the clinician to establish an effective and early therapeutic intervention in order to prevent the occurrence of major complications. These parameters are measurable indices of blood that serve as a marker for disease diagnosis.[7] In this study significant changes were observed involving Packed Cell Volume (PCV), haemoglobin concentration and blood platelet counts; although not with White Blood Cells count where slight variations with malaria-negative cases were observed. The PCV test result showed that 84.38% of the malaria positive patients are anaemic (males:33.67±6.77; females:30.37±6.54), a finding which is concordant with earlier reports.[16,17] Only 15.63% of the malaria negative patients are anaemic. Moreover, haemoglobin concentration values showed that 81.08% of malaria-positive patients are anaemic, with mean haemoglobin concentrations of 11.26±2.26 (male) and 10.1±2.14 (female), with statistical significance at $P<0.05$. These values showed a high occurrence of anaemia in malaria patients than in patients tested negative for malaria. The low mean PCV values in non-malaria cases probably account for the low nutrition status of the subjects in particular, thus reflecting nutrition status of the surrounding populace from which the samples were drawn. This in addition to other factors can affect their immunity state and coincided with the findings of Hill *et al*.[18] who reported that haematological changes related to malaria are subject to variation depending on the level of disease endemicity, nutritional status, genetic factors, sociodemographic conditions, ethnicity and immunity. According to the World Health Organisation Scientific Group 1, the levels of haemoglobin below which anaemia is likely to occur for a population living at sea level are: 11g/dl for children aged six months to six years, 12g/dl for children aged between 6 and 14 years, 13g/dl for adult males, 12g/dl for non-pregnant adult females and 11g/dl for adult pregnant females.[19] Anaemia and thrombocytopenia are the most frequent malaria-associated haematological complications.[20] The pathogenesis of anaemia in malaria is extremely complex, multifactorial and incompletely understood. It is thought to result from a combination of hemolysis of parasitized red blood cells, accelerated removal of both parasitized and innocently unparasitized red blood cells, depressed as well as ineffective erythropoiesis with dyserythropoietic changes and anaemia of chronic disease.[21] The etiology of anemia among parasitized children is thought to be multifactorial; haemolysis of parasitized red blood cells, accelerated removal of both parasitized and non-parasitised red blood cells, depressed and ineffective erythropoiesis due to tumour necrosis factor alpha, anemia of chronic disease, and splenic phagocytosis or pooling.[22,23] Menendez *et al*.[24] reported that malaria-related anaemia is associated with many factors which involve increased destruction and reduced production of red blood cells. Other factors contributing to anaemia in malaria include decreased red blood cells deformability, splenic phagocytosis and/or pooling, hence increasing their rate of clearance from the circulation.[25] Malarial anaemia is usually normocytic and normochromic.[22] However, anaemia associated with malaria can also be microcytic and hypochromic due to the high frequencies of haemoglobinopathies and iron deficiency in endemic countries.[22] During malaria infection, there are soluble derivatives released by the parasite that induce bone marrow dysfunction. These derivatives are therefore implicated in the pathogenesis of malarial anaemia.[26] For *P. vivax* infection, it has been observed that the decrease in haemoglobin concentrations can be attributed to the activity of the parasites.

This work recorded an insignificant change in white blood cell counts in both malaria-positive and malaria-negative patients, irrespective sex and age-group. This finding was in agreement with Maina *et al*.[6] who reported a normal count in malaria cases. Similarly, alterations in the white blood cell counts are less reported and have been associated with factors such as severity, *Plasmodium* species, concurrent infections, and treatment response.[27] On the contrary, leucopenia has been reported in several studies[16,28] as a common finding in malaria, and

McKenzie *et al.*[28] ascribed the leucopenia to the localisation of leucocytes away from the peripheral circulation, splenic sequestration and other marginal pools rather than actual depletion or stasis. Descriptions of leucocytosis and leucopenia in malaria patients have been observed[29] but studies have not shown a specific leucocyte profile alteration in malaria. It has been found that WBC counts are generally lower in malaria patients compared to healthy patients and that there is a trend towards lower WBC counts in patients infected with either *P. falciparum* or *P. vivax*.[30] On a general note, this study revealed a lower white blood cell counts in malaria patients, though the counts are within normal range of white blood cell counts for both sexes.

Variable degree of reduction in circulating platelet counts are consistently reported in malaria.[31] Low platelet count is a characteristic finding of malarial infection and thrombocytopenia may be more common than anaemia in acute malaria infection. Ali *et al.*[32] reported that thrombocytopenia and anaemia are the most common haematological abnormalities observed in malaria and mostly documented in infection with *Plasmodium falciparum*. Moreover, Aggarwal *et al.*[33] reported that thrombocytopenia is a common finding in falciparum infection but rare in *P. vivax*, although thrombocytopenia is usually mild in case of *P. vivax*.[34] In this study, low thrombocyte (Platelets: 190.98±129.1x10^9/L for males; 163.4±99.38 x10^9/L for females) was recorded, it may serve as a strong predictor of malaria, an observation which corroborated many studies.[22,35] In this study, 85.23% of patients with low platelet counts are positive for malaria, contrary to report of high percentage thrombocytopenia in malaria by other investigators; 53.0% and 58.97%.[22,36] This research also showed 38.6% of the patients with normal platelets count are malaria positive and 80% of the patients with thrombocytosis are malaria-positive. The suggested mechanism of thrombocytopenia may be through peripheral destruction[37] excessive removal of platelets by splenic pooling as well as platelet consumption by the process of disseminated intravascular coagulation (DIC).[6] Pain *et al.*[38] suggested that the mechanism of thrombocytopenia in malaria is probably the consequence of several factors including immune factors and the destruction or sequestration of platelets. Antiplatelet antibodies have also been implicated in the pathogenesis of thrombocytopenia.[35] Patients who developed thrombocytopenia due to malaria rarely bleed no matter the degree of reduction in platelets count.[36] In acute malaria infection platelets are found to be hypersensitive and there is increased concentrations of platelet-specific proteins such as beta-thromboglobulin (ßTG) and platelet factor 4 (PF4). Production of thromboxane A_2 and prostacyclin also increased.[21] It has also been postulated that these hypersensitive (hyperactive) platelets will enhance haemostatic responses, and may be the reason for bleeding episodes that rarely occur in acute malarial infections, despite the significant thrombocytopenia.[39]

Conclusion

Changes in haematological parameters due to malaria are a common pathogenetic complication in subjects living in malaria-endemic communities. Although white blood cell counts were not significantly affected the values for the packed cell volume and haemoglobin concentrations indicated an establishment of mild anaemia in concomitance with a significant study population presenting with thrombocytopenia due to *Plasmodium* infection. Malaria is therefore a serious infection having a serious impact on blood cells and haemopoeitic and other systemic processes with cascade of pathophysiology that often have fatal consequences.

Recommendations

Further researches need to be conducted for details on differential blood cell counts, with particular reference to the role of malaria in the development of pathologic thrombocytopenia in the study population. Malaria speciation should be carried out in blood cell profiling to evaluate species-specific haematological changes due to malaria. Improved nutrition through consumption

of fruits and vegetables by malaria patients should be encouraged through public enlightenment programme in order to replenish the low blood cell counts for restoration of health normalcy.

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